40. (Reiterated) The method of claim 39, wherein the bone marrow cell is a hematopoietic stem cell.

41. (Reiterated) The method of claim 40, wherein the hematopoietic stem cell is a lin^- cell or a $CD34^+$ cell.

42. (Amended) The method of claim 38, wherein the peptide comprises SEQ ID NO:4, SEQ ID NO:5, or SEQ ID NO:7.

43. (Amended) The method of claim 38, wherein the peptide consists essentially of SEQ ID NO:4, SEQ ID NO:5, or SEQ ID NO:7.

44. (Reiterated) The method of claim 42, wherein the peptide is covalently linked to a carrier peptide.

45. (Reiterated) The method of claim 44, wherein the carrier peptide is maltose binding protein, glutathione-S-transferase, or a series of six consecutive histidine residues.

46. (Reiterated) The method of claim 38, wherein the subject is treated with a chemotherapeutic agent, and wherein the chemotherapeutic agent is an agent that cross-links DNA, an antimetabolite that inhibits dihydrofolic acid reductase, an inhibitor of cell cycle progression, or a cell-cycle non-specific interstrand DNA crosslinker

47. (Reiterated) The method of claim 46, wherein the chemotherapeutic agent is mafosfamide, etoposide, cisplatinum, methotrexate, cyclophosphamide, a monoclonal antibody, platinum, etoposide, adriamycin, doxorubicin, biCNU, hydroxiurea, taxol, steroids, fluorouracil, viucristine, interferon-alpha, bleomycin, fludarabin, cytokine or a chemokin.

REMARKS

Claims 38, 42, and 43 are amended herein. Claim 38 is amended herein to refer to SEQ ID NO:6, which is amino acids 126-146 of SEQ ID NO:3. Support for the amendment of claim

38 can be found throughout the specification, specifically on page 11, line 11 to page 12, line 13, and on page 39, lines 1 to page 40, line 4, and in original claims 42 and 43. Claims 42 and 43 are amended to correct form. Specifically, claims 42 and 43, which depend from claim 38, are amended to remove the reference to SEQ ID NO:6, which is now recited in claim 38.

No new matter is added. Reconsideration of the subject application is respectfully requested.

Restriction Requirement

In a telephone conference with Examiner Davis on January 8, 2002, Applicants elected Group VI (claims 38-47) with traverse. This election was further asserted in the Preliminary Amendment dated January 9, 2002.

The Office action notes that only if Groups I or II are elected (claims 10-14), an election of a single species must be made (see the office action, page 2, last paragraph). Applicants have elected Group VI, and thus an election of species is not required.

Applicants note that SEQ ID NO:3 is the sequence of amino acid 1 to amino acid 180 of calreticulin. SEQ ID NOs:4-7 are the sequences of particular fragments of SEQ ID NO:3. As noted in the Preliminary amendment, this relationship is clearly delineated in the specification on page 11, line 20 to page 12, line 9. Thus, a search encompassing peptides that consist essentially of 18 consecutive amino acid fragments of SEQ ID NO:3 by definition includes SEQ ID NOs:4-7. In the unlikely event that an election of species is required for group VI, applicants elect Species A, drawn to SEQ ID NO:3, and note that SEQ ID NO:4 is amino acids 103 to amino acid 163 of SEQ ID NO:3; SEQ ID NO:5 is amino acids 120 to amino acid 146 of SEQ ID NO:3; SEQ ID NO:6 is amino acids 129 to 146 of SEQ ID NO:3; and SEQ ID NO:7 is amino acids 129 to amino acid 163 of SEQ ID NO:3. It is further noted that SEQ ID NOs: 4-5 and 7 all comprise SEQ ID NO:6, which is amino acids 129-146 of SEQ ID NO:3.

Rejections Under 35 U.S.C. § 112, first paragraph

Claims 38-47 are rejected under 35 U.S.C. §112, first paragraph, as allegedly the specification does not provide enablement for the use of any peptide of at least 18 amino acids in length of SEQ ID NO:3 to protect a bone marrow cell. Applicants respectfully disagree with this assertion. Applicants note that the Office action states that a method of protecting a bone

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marrow cell using a peptide comprising amino acids 129-146 of SEQ ID NO:3 (also called SEQ ID NO:6 in the specification) or 103-163 of SEQ ID NO:3 (also called SEQ ID NO:4 in the specification) is enabled.

The Office action alleges that undue experimentation would be required to make and test all peptides that include 18 consecutive amino acids in length of SEQ ID NO:3. SEQ ID NO: 3 is 180 amino acids in length. Applicants submit that given the short length of this peptide sequence, one of skill in the art could readily produce all 18-mers from this peptide. For example, automated peptide synthesizers are readily available. Attached as Exhibit A is a set of print-outs on solid phase peptide synthesis, documenting that peptide synthesis is a routine tool. Furthermore, one of skill in the art can readily use molecular genetic techniques to produce peptides. For guidance regarding expression of polypeptides in various host cells, one of skill in the art has a variety of resources (see, e.g., *Molecular Cloning: A Laboratory Manual*, 2nd ed., vol. 1-3, ed. Sambrook *et al.*, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989, and *Current Protocols in Molecular Biology*, ed. Ausubel *et al.*, Greene Publishing and Wiley-Interscience, New York, 1987 (with periodic updates).

Moreover, Applicant has provided methods for screening the peptides to determine of use in protecting bone marrow cells. The assays include an *in vitro* assay for bone marrow proliferation (see the specification at page 33, line 1 to page 37, line 9), as well as an *in vivo* assay for bone marrow protection (see the specification at page 31, line 13 to page 32, line 25). Thus, Applicants submit that given the molecular techniques available, and the guidance provided by the specification, one of skill in the art can readily produce and test all peptides of at least 18 amino acids in length for their ability to protect bone marrow cells.

However, solely to advance the prosecution, and not for reasons pertaining to patentability, Applicants have amended the claims to refer to polypeptides that comprises SEQ ID NO:6 (which is amino acids 129-146 of SEQ ID NO:3). The Office action notes that the specification is enabling for peptides comprising amino acids 129-146 of SEQ ID NO:3 (see the Office action page 4, point 2). Applicant submits that the amendment of claim 38 to refer to SEQ ID NO: 6 removes the rejection.

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Cited References

Applicants thank Examiner Davis for returning the signed PTO-1449, and note that no additional prior art was cited.

Conclusion

Applicants submit that claims 38-47 are now in condition for allowance. If any minor matters remain to be addressed before a Notice of Allowance is issued, the Examiner is invited to contact the undersigned at the phone number listed below.

Respectfully submitted,

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Marked-up Version of Amended Claims
Pursuant to 37 C.F.R. §§ 1.121(b)-(c)

38. (Twice Amended) A method of protecting a bone marrow cell in a subject treated with a chemotherapeutic agent or radiation from a toxicity caused by chemotherapy or irradiation, comprising administering to the subject a therapeutically effective amount of a peptide comprising [at least 18 consecutive amino acids of SEQ ID NO:3] SEQ ID NO:6, thereby stimulating proliferation of the bone marrow cell or [the] protecting the bone marrow cell from the toxicity caused by chemotherapy or irradiation.

39. (Reiterated) The method of claim 38, wherein the hematopoietic cell is a bone marrow cell.

40. (Reiterated) The method of claim 39, wherein the bone marrow cell is a hematopoietic stem cell.

41. (Reiterated) The method of claim 40, wherein the hematopoietic stem cell is a lin^- cell or a $CD34^+$ cell.

42. (Amended) The method of claim 38, wherein the peptide comprises SEQ ID NO:4, SEQ ID NO:5, [SEQ ID NO:6] or SEQ ID NO:7.

43. (Amended) The method of claim 38, wherein the peptide consists essentially of SEQ ID NO:4, SEQ ID NO:5, [SEQ ID NO:6] or SEQ ID NO:7.

44. (Reiterated) The method of claim 42, wherein the peptide is covalently linked to a carrier peptide.

45. (Reiterated) The method of claim 44, wherein the carrier peptide is maltose binding protein, glutathione-S-transferase, or a series of six consecutive histidine residues.

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46. (Reiterated) The method of claim 38, wherein the subject is treated with a chemotherapeutic agent, and wherein the chemotherapeutic agent is an agent that cross-links DNA, an antimetabolite that inhibits dihydrofolic acid reductase, an inhibitor of cell cycle progression, or a cell-cycle non-specific interstrand DNA crosslinker.

47. (Reiterated) The method of claim 46, wherein the chemotherapeutic agent is mafosfamide, etoposide, cisplatinum, methotrexate, cyclophosphamide, a monoclonal antibody, platinum, etoposide, adriamycin, doxorubicin, biCNU, hydroxiurea, taxol, steroids, fluorouracil, viucristine, interferon-alpha, bleomycin, fludarabin, cytokine or a chemokin.